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By: _____
Neely Jo Entwistle

PATENT
Customer No. 22,852
Attorney Docket No. 09367-0052.00000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
VAISBERG, Eugeni A. et al.	Group Art Unit: 1631
Application No.: 09/311,996	Examiner: BRUSCA, John S.
Filed: May 14, 1999	
For: DATABASE SYSTEM INCLUDING COMPUTER FOR PREDICITVE CELLULAR BIOINFORMATICS	Confirmation No.: 1991

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Sir:

APPEAL BRIEF UNDER BOARD RULE § 41.37

In support of the Notice of Appeal filed June 15, 2005, and further to Board Rule 41.37, Appellants present this brief and enclose herewith a check for the fee of $500.00 required under 37 C.F.R. § 41.20(b).

This Appeal responds to the March 10, 2005 final rejection of claims 49-57, 60, 61, and 63-66.

If any additional fees are required or if the enclosed payment is insufficient, Appellant requests that the required fees be charged to Deposit Account No. 06-0916.

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Table of Contents

Real Party In Interest

Cytokinetics, Inc. is the real party in interest.

Related Appeals and Interferences

There are currently no other appeals or interferences of which Appellants, Appellants' legal representative, or Assignee are aware, that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

Status of Claims

Claims 49-57, 60, 61, and 63-66 are currently pending in this application. The rejections of claims 49-57, 60, 61, and 63-66 are currently being appealed.

Status of Amendments

No claim has been amended subsequent to the final rejection.

Summary of Claimed Subject Matter

The present application contains three independent claims: claims 49, 56, and 63.

Independent claim 49 is directed to a computer program product for determining a property of a manipulation based upon determination of effects of said manipulation on a plurality of different cell types, said computer program product comprising:

code for receiving one or more images of a plurality of components of a plurality of cells, wherein said plurality of cells are of different cell types and wherein said plurality of cells have been exposed to the manipulation;

code for determining a plurality of features of said plurality of components of said plurality of cells of different cell types;

code for analyzing said plurality of features to yield a plurality of descriptors, wherein some of said features are from a first cell type and some of said features are from a second cell type, and wherein some of said features from a first cell type are combined with features from a second cell type to yield one or more composite descriptors;-

code for performing principal component analysis on said plurality of descriptors wherein at least one of said plurality of descriptors is a composite descriptor, whereby said descriptors are reduced to yield a fingerprint;

code for determining properties of said manipulation based upon said principal component analysis; and

a computer readable storage medium comprising said computer program product.

Claim 50 is dependent on claim 49 and is directed to the computer program product of claim 49 wherein said plurality of components are selected from a protein, a protein modification, a nucleic acid, a lipid, a carbohydrate, a sub-cellular structure, and an organelle.

Claim 51 is dependent on claim 49 and is directed to the computer program product of claim 49 wherein said manipulation comprises applying a chemical factor.

Claim 52 is dependent on claim 49 and is directed to the computer program product of claim 49 wherein said property comprises toxicity.

Claim 53 is dependent on claim 49 and is directed to the computer program product of claim 49 wherein said property comprises a mechanism of action.

Claim 54 is dependent on claim 49 and is directed to the computer program product of claim 49 wherein said property comprises at least one of a plurality of pharmacological properties.

Claim 55 is dependent on claim 54 and is directed to the computer program product of claim 54 wherein said pharmacological properties comprises at least of absorption, excretion, distribution, and metabolism.

Independent claim 56 is directed to a computer program product comprising a machine readable medium on which is provided program instructions for determining an effect of a manipulation on a plurality of cells of different cell types, the instructions comprising:

code for receiving one or more images of a plurality of components of a plurality of cells, wherein said plurality of cells are of different cell types and wherein said plurality of cells have been exposed to the manipulation;

code for determining a plurality of features of said plurality of components of said plurality of cells of different cell types;

code for combining said plurality of features

wherein some of said features are from a first cell type and some of said features are from a second cell type, and

wherein some of said features from a first type are combined with features from a second cell type to yield one or more composite features; and

code for performing statistical analysis on said plurality of features wherein said statistical analysis comprises multidimensional representations, principal component analysis, or frequency based representations on at least said one or more composite features to determine the effect of the manipulation on the plurality of cells.

Claim 57 is dependent on claim 56 and is directed to the computer program product of claim 56, wherein the manipulation is application of at least one of a chemical factor, a biological factor, an electromagnetic factor, a gravitational factor, a mechanical factor, a thermal factor, a temporal factor, and a nuclear factor.

Claim 60 is dependent on claim 56 and is directed to the computer program product of claim 56, wherein said first component is a protein, a protein modification, a nucleic acid, a lipid, a carbohydrate, a sub-cellular structure or an organelle.

Claim 61 is dependent on claim 56 and is directed to the computer program product of claim 56, wherein the effect of the manipulation is at least one of the

following: toxicity, specificity against a subset of tumors, a mechanism of chemical activity, a mechanism of biological activity, interaction with a target protein, an adverse biological effect, an adverse clinical effect, cellular availability, a pharmacological property, a gene expression profile, absorption, excretion, distribution, metabolism, and a pharmacodynamic effect.

Independent claim 63 is directed to a computer program product comprising a machine readable medium on which is provided program instructions for predicting properties of a chemical compound based on information about effects of at least one of a plurality of known compounds on a plurality of cells of different cell types, the instructions comprising:

code for receiving one or more images of a plurality of components of a plurality of cells of different cell types that have been exposed to the chemical compound;

code for determining, from the one or more images, multiple descriptors for multiple components of the plurality of cells of said different cell lines,

wherein said code for determining a multiple descriptors comprises code for performing principal component analysis on the said multiple descriptors,

wherein said descriptors are determined for at least two different cell lines and

wherein at least some of said descriptors combine features from cells of different cell types;

code for determining a relationship between said descriptors of said chemical compound with other descriptors of said known compounds; and

code for making an inference about said chemical compound based upon said other descriptors,

wherein said descriptors and other descriptors comprise numeric or logical values.

Claim 64 is dependent on claim 63 and is directed to the computer program product of claim 63, wherein the multiple components are independently selected from the group consisting of a protein, a protein modification, a nucleic acid, a lipid, a carbohydrate, a sub-cellular structure or an organelle.

Claim 65 is dependent on claim 63 and is directed to the The computer program product of claim 63, wherein the property that is being predicted is at least one of the following: toxicity, specificity against a subset of tumors, a mechanism of chemical activity, a mechanism of biological activity, interaction with a target protein, an adverse biological effect, an adverse clinical effect, cellular availability, a pharmacological property, a gene expression profile, absorption, excretion, distribution, metabolism, and a pharmacodynamic effect.

Claim 66 is dependent on claim 49 and is directed to the computer program product of claim 49 wherein said manipulation is selected from the group consisting of applying a hormone, applying a growth factor, applying an extracellular matrix component, applying a virus, electroporation, applying an antisense polynucleotide, a gene knock-out, a gene overexpression, a gene mutation, a cell fusion, and combinations thereof.

Grounds of Rejection

A. Claims 49-57, 60, 61, and 63-66 stand rejected under 35 U.S.C. § 112, first paragraph, for containing subject matter which was not described in the specification in a such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

B. Claims 49-57, 60, 61, and 63-65 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Pauwels, et al., Journal of Pharmacological and Toxicological Methods, Vol. 37, pages 105-115 (1997) ("Pauwels") in light of Paull et al., Journal of the National Cancer Institute, Vol. 81 pages 1088-1092 (1989) ("Paull")

C. Claims 63 and 66 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Pauwels in view of Paull, and further in view of Rojanasakul et al., Advanced Drug Delivery Reviews Vol. 18, pages 115-131 (1996) ("Rojanasakul").

Argument

1. Rejection under 35 U.S.C. § 112

Claims 49-57, 60, 61, and 63-66 stand rejected under 35 U.S.C. § 112, first paragraph, for containing subject matter which was not described in the specification in a such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

(a) Rejection of claims 49-57, 60, 61, and 63-66

The Office Action mailed on March 10, 2005 states that Applicants' "specification does not describe composite descriptors or descriptors which comprise features of different cell types. The Office Actio further indicates that

> "Applicant's arguments...have been fully considered but they are not persuasive. The applicants point to a number of passages in the specification in support of written description of composite descriptors, most notably at page 24, lines 17 - 19. The applicants further state that some of the support is generic to composite descriptors. However none of the pointed to passages explicitly describes the claimed species of descriptor that is a composite descriptor comprising features of two different cell types."

Office Action mail on March 10, 2005, page 3 paragraph 5.

Applicants respectfully traverse. There is no legal requirement for explicit description. The test for written description and enablement is whether the applicants' specification contains "a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art ... to make and use the same...." 35 U.S.C. § 112.

> As a matter of Patent Office practice... a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of §112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. In re Marzocchi, 439 F.2d 220, 223-24, 169 U.S.P.Q. 367, 369-70 (CCPA 1971).

MPEP 2107.2(III)(A)

Further the court in *Marzocchi* has stated, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." MPEP 2164.04; In re Marzocchi, 439 F.2d 220, 169 U.S.P.Q. 367 (CCPA 1971).

Applicants first respectfully assert that the definition of "descriptors" in the specification is not as narrow as it was apparently understood by the Office. The instant specification stated that descriptors "can be formed by combining features of two or more cell components as identified using the markers." *See, e.g.,* page 3, line 7 of Applicants' specification. Contrary to the Office's impression that the descriptors can only be formed from features originating from the same cell lines, this definition did not limit the source of these features. Indeed, this description embraces descriptors that combine features from either the same type of cells or from different types of cells.

Furthermore, in Applicants' amendment to the specification on August 9, 2004, Applicants properly incorporated the passage "[i]n some embodiments, the descriptors include features from different cell portions or cell types." *See* page 12, line 27 of

Applicants' specification. While the Office correctly interpreted the passage to mean that a group of descriptors may include information derived from different cell types, this interpretation is by no means complete. Read in its entirety, this passage takes account of not only the situation where multiple descriptors include information derived from different cell types, but also the situation where a single descriptor includes information derived from different cell types.

Applicants next assert that explicit support is found in multiple places within the specification for "features from a first cell type are combined with features from a second cell type to yield one or more composite descriptors." The instant specification illustrates the relationship among "markers," "features" and "descriptors" this way: "[d]escriptors can be formed by combining features of 2 or more cell components as identified using the markers." *See* page 3, line 8-9 of Applicants' specification. Stated differently, cell features like cell components and morphological characters can be identified using the markers, and the markers can then be combined to make descriptors. The following passage are also found in Applicants' specification as indicated:

On page 24, line 17-19: (*emphasis added*).	**a descriptor** (or a fingerprint) **is** described as **"[a] vector of two or more ... scalar values** extracted from **a plurality of cell lines** and markers grown in the same condition," whereas "scalar values" are extracted from fluorescence images (i.e., the markers) taken from cell populations.
On page 28, lines 1-6, (*emphasis added*)	**"descriptors" were built by "quantifying and/or qualifying patterns of each marker in the cell lines** under study" and such studies were performed by "growing **multiple cell lines** in the presence of multiple compounds, or substances." (*Emphasis added*).

On page 18, line 28, to page 19, line 4, (*emphasis added*).	Applicants describes making "**one** or more types of **numerical descriptors**" from values obtained from regional "fluorescence patterns of markers in **multiple cell lines** in the presence and absence of compounds." Such "regional" patterns can include "determining one or more regions from around nuclei, individual cells, organelles, and the like."

Therefore, any one descriptor may include information extracted from markers, which in turn identify features from multiple cell lines. The instant specification thus adequately supports the claims. The Office fails to "explain why it doubts the truth or accuracy of any" of the statements found in Applicants specification. And furthermore, the Office does not "back up its assertions with acceptable evidence or reasoning."

Applicants hereby respectfully request the Examiner withdraw this rejection under 35 U.S.C. § 112, first paragraph.

2. Rejection under 35 U.S.C. § 103(a) over Pauwels in view of Paull

Claims 49-57, 60, 61, and 63-65 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Pauwels, in light of Paull.

(a) Rejection of claims 49-57, 60, 61, and 63-65

The Office acquiesced in Applicants' argument that Pauwels did not alone suggest or render obvious the instant claims because it "does not show descriptors or fingerprints that comprise information of a plurality of cell lines." *See* page 6, lines 5-6 of Office Action, dated September 24, 2004; *see also* page 4, paragraph 10 of Office

Action, dated May 10, 2004; page 8, lines 3-7 of Amendment G, filed April 6, 2004. However, the Office asserts that Pauwels described using digital images of treated cells to differentiate the effect of antitumor drugs on tumor cell lines, and that Paull depicted a computer program called COMPARE that clusters antitumor drugs by profiling growth inhibition of 60 tumor cells. The Office alleges that at the time of the invention, a person of ordinary skill in the art would find it obvious to write a computer program according to Pauwels, and then modify it in order to fingerprint drugs according to Paull. Applicants respectfully disagree.

A *prima facie* case of obviousness requires the Office to cite to a reference or combination of references that (a) discloses all the elements of the claimed invention, (b) suggests or motivates one of skill in the art to combine or modify those elements to yield the claimed combination, and (c) provides a reasonable expectation of success should the claimed combination be carried out (*See, e.g., Northern Telecom Inc. v. Datapoint Corp.*, 908 F.2d 931, 15 U.S.P.Q.2d 1321, 1323 (Fed. Cir. 1990); and *In re Dow Chemical Co.*, 837 F.2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988)). Failure to establish **any one** of these three requirements precludes a finding of a *prima facie* case and, without more, entitles applicant to allowance of the claims at issue. As stated in *In re Dow Chemical Co.:*

> The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art.... Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure.

In re Dow Chemical Co., 837 F.2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988)

The Federal Circuit has held that "[t]here are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." *In re Rouffet*, 149 F.3d 1350, 1357, 47 U.S.P.Q.2d 1452, 1458 (Fed. Cir. 1998). *See also* M.P.E.P. § 2143. The Federal Circuit has also held that the evidence of a teaching, suggestion, or motivation to modify or combine must be "clear and particular." *See In re Dembiczak*, 175 F. 3d 994, 999, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). Both the suggestion or motivation and the reasonable expectation of success must be found in the prior art. *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q. 2d 1438, 1442 (Fed. Cir. 1991). Motivation may be lacking when the state of the art at the time pointed researchers in a different direction than the one undertaken by the inventor. *In re Hedges*, 783 F. 2d 1038, 1041, 228 U.S.P.Q. 685, 688 (Fed. Cir. 1986); *Gore v. Garlock*, 721 F. 2d 1540, 1552, 220 U.S.P.Q. 303 (Fed. Cir. 1983). Indeed, the Federal Circuit has repeatedly recognized that proceeding contrary to the accepted wisdom in the art represents strong evidence of non-obviousness. *Id.*

An explicit statement in the prior art reference that a certain modification does not work certainly constitutes "teaching away." It would also remove any reasonable expectation that such a modification would lead to likely success.

Not only does Pauwels provide no suggestion of using the COMPARE program, known in the literature for at least 8 years, but Pauwels actually teaches away from the combination of these technologies. As the Examiner has pointed out, Paull described using COMPARE to analyze the inhibitory effect of antitumor drugs on the growth of tumor cell lines. Paull described this program in the literature in 1989.

Pauwels (published in 1997, eight years after Paull) attempted to use a **single-variant approach, just like the one taught by Paull,** and found that it "**do[es] not enable the pharmacological classes of the drugs to be distinguished one from another**" and that "it was **necessary to combine the information on the 15 parameters** into one calculation step ...." *See* Pauwels, page 109, lines 10-15. The result of an experiment similar to the one reported by Paull was listed on page 108 in Figure 1. According to this figure, different classes of drugs often inhibited cell proliferation or growth to the same extent among the three typical tumor cell lines, MXT, J82, and T24. From this set of cell-proliferation data, the authors were only able to conclude that aside from the drug CPA, (which had shown no cytotoxic effect), "all the other drugs had significant cytotoxic effect on cell proliferation." *See* Pauwels, page 108, lines 10-13.

The MXT CELL LINE profile further illustrates this point. According to Table 1 (Pauwels, page 106), the drug Cisplatin (CDDP) belongs to class ALK, 5-Fluorouracile (5-FU) and 6-Mercaptopurine (MP) belong to class AM, and Doxorubicin (DOX) belongs to class NDID, but the proliferation profiles for each of these drugs are remarkably similar, if not identical, when measuring growth inhibition on the of the MXT cell line. Figure 1 provides numerous examples of drugs from different pharmacological classes that exert the same growth inhibition effect on different cell lines. Accordingly, Pauwels **sensibly cautioned persons skilled in the art to avoid the single-parameter method** taught by Paull, if the goal is to distinguish cell-drug interaction. *See* Pauwels, page 109, lines 10-15. Even Paull discloses that, using its reported method, drugs from different classes would often rank higher than drugs from

the same classes or than drugs otherwise more closely related. *See* Paull, page 1092, lines 2-6.

Pauwels alone does not render the instant claims obvious because this reference does not teach or suggest descriptors or fingerprints that comprise information of a plurality of cell lines. Likewise, Paull alone does not render the instant claims obvious because this reference teaches the use of the COMPARE program to analyze drug effects on only a single variant across cell lines.

There is no motivation found in either reference to combine their teachings. In fact, Pauwels teaches away from Paull by cautioning those trying to distinguish cell-drug interaction to avoid a single-parameter method such as that taught by Paull.

Finally, even if the teachings of Pauwels and Paull were combined, the person of ordinary skill in the art would have no reasonable expectation of success in using Paull's single variant approach when Pauwels teaches that it is "necessary to combine the information on the 15 parameters into one calculation step" in order to "enable the pharmacological classes of the drugs to be distinguished one from another."

Accordingly, the Examiner has not met his burden of establishing a prima facie case of obviousness and reversal of the rejection of claims 49-57, 60, 61, and 63-65 is respectfully requested.

3. Rejection under 35 U.S.C. § 103(a) over Pauwels and Paull in view of Rojanasakul

Claims 63 and 66 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Pauwels in view of Paull, and further in view of Rojanasakul. Appellants respectfully disagree.

(a) Rejection of claims 63 and 66

Initially, Applicants would like to reiterate that claim 63 is not currently directed to antisense oligonucleotides. The obviousness rejection in view of Rojanasakul was therefore improperly imposed upon claim 63.

According to the Office, Rojanasakul suggests that antisense oligonucleotides could be used to modulate gene expression and may be potentially useful for disease therapies. The Office further alleges that such a use would suggest to a person skilled in the art to modify the computer program taught by Pauwels. Applicants respectfully disagree.

A *prima facie* case of obviousness requires the Office to cite to a reference or combination of references that (a) discloses all the elements of the claimed invention, (b) suggests or motivates one of skill in the art to combine or modify those elements to yield the claimed combination, and (c) provides a reasonable expectation of success should the claimed combination be carried out (*See, e.g., Northern Telecom Inc. v. Datapoint Corp.*, 908 F.2d 931, 15 U.S.P.Q.2d 1321, 1323 (Fed. Cir. 1990); and *In re Dow Chemical Co.*, 837 F. 2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988)). Failure to establish **any one** of these three requirements precludes a finding of a *prima facie*

case and, without more, entitles applicant to allowance of the claims at issue. As stated in *In re Dow Chemical Co.*::

> The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art.... Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure.

In re Dow Chemical Co., 837 F. 2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988)

The Federal Circuit has held that "[t]here are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." *In re Rouffet*, 149 F. 3d 1350, 1357, 47 U.S.P.Q.2d 1452, 1458 (Fed. Cir. 1998). *See also* M.P.E.P. § 2143. The Federal Circuit has also held that the evidence of a teaching, suggestion, or motivation to modify or combine must be "clear and particular." *See In re Dembiczak*, 175 F.3d 994, 999, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). Both the suggestion or motivation and the reasonable expectation of success must be found in the prior art. *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q. 2d 1438, 1442 (Fed. Cir. 1991). Motivation may be lacking when the state of the art at the time pointed researchers in a different direction than the one undertaken by the inventor. *In re Hedges*, 783 F. 2d 1038, 1041, 228 U.S.P.Q. 685, 688 (Fed. Cir. 1986); *Gore v. Garlock*, 721 F. 2d 1540, 1552, 220 U.S.P.Q. 303 (Fed. Cir. 1983).

As discussed above, Pauwels teaches the classification of drugs by evaluation of the effect of a drug on at least 15 cell parameters in a single cell line. Paull teaches the use of the COMPARE program to evaluate the effects of a drug on a single cell parameter across several cell lines. Rojanasakul teaches the use of antisense

oligonucleotides to modulate gene expression and to treat diseases. None of the cited references, Pauwels, Paull or Rojanasakul, teach a computer program product for determining the effects of a manipulation on a plurality of different cell types, by performing principal component analysis on a plurality of descriptors comprising at least one composite descriptor, by imaging and analyzing a plurality of features to yield a plurality of descriptors, wherein some of the features are from a first cell type and some of the features are from a second cell type, and wherein some of the features from the first cell type are combined with features from the second cell type to yield one or more composite descriptors.

For the reasons discussed above, Pauwels and Paull do not render the instant claims obvious either alone or in combination. Neither of these references explicitly or implicitly suggests the combination of their methods with the antisense oligonucleotides of Rojanasakul. Rojanasakul, likewise provides no motivation to combine its teachings with the teachings of Pauwels and/or Paull. Indeed, the only place where any suggestion to combine antisense oligonucleotides and descriptors can be found is in Applicants' specification.

Even if the teachings of these references are combined, the deficiencies of Pauwels in view of Paull are not rectified by Rohanasakul because Rohanasakul does not provide the required motivation to combine Pauwels and Paull or any expectation of success if combining these teachings.

Accordingly, the Examiner has not met his burden of establishing a prima facie case of obviousness and reversal of the rejection of claims 63 and 66 is respectfully requested.

Conclusion

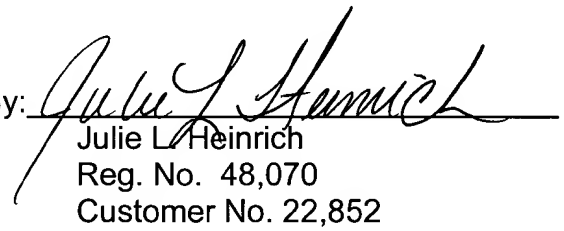
For the reasons given above, pending claims 49-57, 60, 61, and 63-65 are allowable and reversal of the Examiner's rejections is respectfully requested.

To the extent any extension of time under 37 C.F.R. § 1.136 is required to obtain entry of this Appeal Brief, such extension is hereby respectfully requested. If there are any fees due under 37 C.F.R. §§ 1.16 or 1.17 which are not enclosed herewith, including any fees required for an extension of time under 37 C.F.R. § 1.136, please charge such fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: August 12, 2005

By: 
Julie L. Heinrich
Reg. No. 48,070
Customer No. 22,852

Claims Appendix to Appeal Brief Under Rule 41.37(c)(1)(viii)

1-48. (Cancelled)

49. (Previously Presented) A computer program product for determining a property of a manipulation based upon determination of effects of said manipulation on a plurality of different cell types, said computer program product comprising:

code for receiving one or more images of a plurality of components of a plurality of cells, wherein said plurality of cells are of different cell types and wherein said plurality of cells have been exposed to the manipulation;

code for determining a plurality of features of said plurality of components of said plurality of cells of different cell types;

code for analyzing said plurality of features to yield a plurality of descriptors, wherein some of said features are from a first cell type and some of said features are from a second cell type, and wherein some of said features from a first cell type are combined with features from a second cell type to yield one or more composite descriptors;-

code for performing principal component analysis on said plurality of descriptors wherein at least one of said plurality of descriptors is a composite descriptor, whereby said descriptors are reduced to yield a fingerprint;

code for determining properties of said manipulation based upon said principal component analysis; and

a computer readable storage medium comprising said computer program product.

50. (Previously Presented) The computer program product of claim 49 wherein said plurality of components are selected from a protein, a protein modification, a nucleic acid, a lipid, a carbohydrate, a sub-cellular structure, and an organelle.

51. (Previously Presented) The computer program product of claim 49 wherein said manipulation comprises applying a chemical factor.

52. (Previously Presented) The computer program product of claim 49 wherein said property comprises toxicity.

53. (Previously Presented) The computer program product of claim 49 wherein said property comprises a mechanism of action.

54. (Previously Presented) The computer program product of claim 49 wherein said property comprises at least one of a plurality of pharmacological properties.

55. (Previously Presented) The computer program product of claim 54 wherein said pharmacological properties comprises at least of absorption, excretion, distribution, and metabolism.

56. (Previously Presented) A computer program product comprising a machine readable medium on which is provided program instructions for determining an effect of a manipulation on a plurality of cells of different cell types, the instructions comprising:

code for receiving one or more images of a plurality of components of a plurality of cells, wherein said plurality of cells are of different cell types and wherein said plurality of cells have been exposed to the manipulation;

code for determining a plurality of features of said plurality of components of said plurality of cells of different cell types;

code for combining said plurality of features

wherein some of said features are from a first cell type and some of said features are from a second cell type, and

wherein some of said features from a first type are combined with features from a second cell type to yield one or more composite features; and

code for performing statistical analysis on said plurality of features wherein said statistical analysis comprises multidimensional representations, principal component analysis, or frequency based representations on at least said one or more composite features to determine the effect of the manipulation on the plurality of cells.

57. (Previously Presented) The computer program product of claim 56, wherein the manipulation is application of at least one of a chemical factor, a biological factor, an electromagnetic factor, a gravitational factor, a mechanical factor, a thermal factor, a temporal factor, and a nuclear factor.

58. (Cancelled)

59. (Cancelled)

60. (Previously Presented) The computer program product of claim 56, wherein said first component is a protein, a protein modification, a nucleic acid, a lipid, a carbohydrate, a sub-cellular structure or an organelle.

61. (Previously Presented) The computer program product of claim 56, wherein the effect of the manipulation is at least one of the following: toxicity, specificity against a subset of tumors, a mechanism of chemical activity, a mechanism of biological activity, interaction with a target protein, an adverse biological effect, an adverse clinical effect, cellular availability, a pharmacological property, a gene expression profile, absorption, excretion, distribution, metabolism, and a pharmacodynamic effect.

62. (Cancelled)

63. (Previously Presented) A computer program product comprising a machine readable medium on which is provided program instructions for predicting properties of a chemical compound based on information about effects of at least one of a plurality of known compounds on a plurality of cells of different cell types, the instructions comprising:

code for receiving one or more images of a plurality of components of a plurality of cells of different cell types that have been exposed to the chemical compound;

code for determining, from the one or more images, multiple descriptors for multiple components of the plurality of cells of said different cell lines,

wherein said code for determining a multiple descriptors comprises code for performing principal component analysis on the said multiple descriptors,

wherein said descriptors are determined for at least two different cell lines and

wherein at least some of said descriptors combine features from cells of different cell types;

code for determining a relationship between said descriptors of said chemical compound with other descriptors of said known compounds; and

code for making an inference about said chemical compound based upon said other descriptors,

wherein said descriptors and other descriptors comprise numeric or logical values.

64. (Previously Presented) The computer program product of claim 63, wherein the multiple components are independently selected from the group consisting of a protein, a protein modification, a nucleic acid, a lipid, a carbohydrate, a sub-cellular structure or an organelle.

65. (Previously Presented) The computer program product of claim 63, wherein the property that is being predicted is at least one of the following: toxicity, specificity against a subset of tumors, a mechanism of chemical activity, a mechanism

of biological activity, interaction with a target protein, an adverse biological effect, an adverse clinical effect, cellular availability, a pharmacological property, a gene expression profile, absorption, excretion, distribution, metabolism, and a pharmacodynamic effect.

66. (Previously Presented) The computer program product of claim 49 wherein said manipulation is selected from the group consisting of applying a hormone, applying a growth factor, applying an extracellular matrix component, applying a virus, electroporation, applying an antisense polynucleotide, a gene knock-out, a gene overexpression, a gene mutation, a cell fusion, and combinations thereof.

Evidence Appendix to Appeal Brief Under Rule 41.37(c)(1)(ix)

No evidence is being cited herein.

Related Proceedings Appendix to Appeal Brief Under Rule 41.37(c)(1)(x)

There are currently no other related appeals or interferences, of which appellants, appellants' legal representative, or assignee are aware. Accordingly, there are no decisions from related proceedings cited herein.

08-15-5

A.F.

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I hereby certify that this correspondence is being deposited with the United States Postal Services "Express Mail Post Office to Addressee" service under 37 CFR § 1.10 on the date indicated above and is addressed to: Mail Stop Appeal Brief-Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

By: Neely Jo Entwistle

PATENT
Customer No. 22,852
Attorney Docket No. 09367-0052.00000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
VAISBERG, Eugeni A. et al.	Group Art Unit: 1631
Application No.: 09/311,996	Examiner: BRUSCA, John S.
Filed: May 14, 1999	
For: DATABASE SYSTEM INCLUDING COMPUTER FOR PREDICITVE CELLULAR BIOINFORMATICS	Confirmation No.: 1991

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

TRANSMITTAL OF APPEAL BRIEF UNDER BOARD RULE 41.37

Transmitted herewith is the APPEAL BRIEF in this application with respect to the Notice of Appeal filed on June 15, 2005.

This application is on behalf of

☐ Small Entity ☒ Large Entity

Pursuant to 37 C.F.R. 41.20(b)(2), the fee for filing the Appeal Brief is:

☐ $250.00 (Small Entity)

☒ $500.00 (Large Entity)

TOTAL FEE DUE:

Notice of Appeal Fee	$ 500.00
Extension Fee (if any)	$
Total Fee Due	$ 500.00

☒ Enclosed is a check in the amount of $500.00 in payment of the above fees.

PETITION FOR EXTENSION. If any extension of time is necessary for the filing of this Appeal Brief, and such extension has not otherwise been requested, such an extension is hereby requested, and the Commissioner is authorized to charge necessary fees for such an extension to our Deposit Account No. 06-0916.

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: August 12, 2005

By: Julie L. Heinrich

Julie L. Heinrich
Reg. No. 48,070
Customer No. 22,852